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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,247	07/02/2007	Foo Yew Liew	0380-P04195US00	7364

110 7590 05/19/2008

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EXAMINER	
MERTZ, PREMA MARIA	

ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
05/19/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,247	LIEW ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 15-31* is/are pending in the application.

4a) Of the above claim(s) *1-11, 18-20 and 21-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12 and 15-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/25/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II (claims 12, 15-20; species arthritis) on 3/26/2008 is acknowledged. The traversal is on the ground(s) that the restriction is improper because Group I (claims 1-11) should be examined with Group II (claims 12, 15-20) because claims 1-11 recite no requirement for performing the methods in vitro. However, contrary to Applicants arguments, claim 11 which depends from independent claim 1, recites further contacting the regulatory T cell with a substance capable of stimulating signaling through the cell's T cell receptor. In the specification, page 4, lines 14-22, recite that a T cell stimulus is normally provided to the T regulatory cells along with the EBI3-p35 but in vivo such administration of a substance is not required because the T regulatory cells in the body will normally receive sufficient TCR stimulus from their environment in vivo and so will proliferate solely on administration of EBI3-p35. Therefore, claims 1-11 are drawn to an in vitro method while claims 12, 15-20 are drawn to an in vivo method. Therefore, contrary to Applicants arguments, Group I (claims 1-11) are drawn to an in vitro method having different starting materials, cell populations, results steps and method steps compared to Group II (claims 12, 15-20) drawn to an in vivo method.

Since the methods of Groups I-II are patentably distinct from each other because each recites method steps not required by the other, each method uses different starting materials and cell populations, the search of both methods in one patent application would result in an undue search burden.

The Groups as delineated in the restriction requirement 1/28/2008 are patentably distinct one from the other such that each invention could, by itself, in principle, support its own separate patent (as shown by the arguments put forth in the written restriction requirement).

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-11, 18-20 (non-elected species) and 21-31 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 12, 15-17 are drawn to the elected species and are under consideration by the Examiner.

Claim Rejections - 35 USC § 112, first paragraph, scope of enablement

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2a. Claims 12, 15-17, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating rheumatoid arthritis or attenuating established arthritis in a subject by administering an effective amount of EBI3-35 to enhance regulatory T cell activity in the subject, does not reasonably provide enablement for a method of as recited in claim 12. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are drawn very broadly to methods of enhancing regulatory T cell activity in a subject without the recitation of the condition in which the enhanced activity is required. The specification, page 26, lines 9-12, recites:

"We have tested the effect of EBI3-p35-Fc in the collagen-induced arthritis (CIA) model in the mouse using an established protocol (Leung BP *et al. J. Immunol.* 170:1524, 2003)."

The specification, page 26, lines 25-28, recites:

"Fig. 6 shows that control mice treated with PBS developed the expected disease (incident and clinical score), whereas those treated with EBI3-p35-Fc showed minimum disease symptom. While the control mice became malaise and showed significant weight loss, the treated mice remained healthy and show normal weight gain."

The specification, page 27, lines 5-9, recites:

"As shown in Fig. 8, EBI3-p35-Fc is effective in attenuating ongoing CIA when injected intraperitoneally on day 27 of the experiment when the disease is already established. Furthermore, EBI3-p35-Fc is as effective as sIL-15Rα or Enbrel in the treatment of CIA."

However, other than the examples on pages 26-27, which demonstrate that administration of EBI3-p35-Fc in the CIA model results in treatment of rheumatoid arthritis, the specification fails to provide any guidance for the successful treatment of all the other possible conditions requiring enhanced regulatory T cell activity.

By application of the factors set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) quantity of experimentation, (2) guidance presented, (3) the

predictability of the art, and (4) the breadth of the claims, in the instant application, the quantity of experimentation to determine which types of conditions requiring enhancing regulatory T cell activity are encompassed by the scope of the claims is practically infinite and the guidance provided in the specification very little, thereby rendering the results of the methods taught in the specification unpredictable (see pages 26-27). Therefore, it would require undue experimentation to determine which types of conditions, would be encompassed by the scope of the method claims. The disclosure of the methods described on pages 26-27 is clearly insufficient support under the first paragraph of 35 U.S.C. 112 for claims, which encompass a method of enhancing regulatory T cell activity in all conditions. In In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), the Courts have held that:

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since some improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that the scope of the claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological

activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Therefore, there are substantial scientific reasons to doubt the scope of enablement, as set forth above. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe treatment of any other conditions other than treatment of rheumatoid arthritis by administering EBI3-p35 cytokine and since it is deemed to constitute undue experimentation to determine all the other types of conditions that could be treated with EBI3-p35, the disclosure is not commensurate with the scope of the claims. It is suggested that by employing conventional claim language, the method claims be amended to include the specific condition supported by the instant specification.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Given the inherent unpredictability of physiological activity, which would include biological processes, i.e., methods of treatment, a certain amount

of enablement beyond mere assertion must be required.

The CAFC decision (Genentech Inc. v. Novo Nordisk, 42 USPQ2d 1001, 1997) expressly states that:

"When there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

In the instant case, a method of treating rheumatoid arthritis, is very different from a method of treating multiple sclerosis. Furthermore, the limited results presented for treatment of rheumatoid arthritis, are not sufficient to enable the breadth of the claims and are not predictive of in vivo efficacy for treatment of all the other types of conditions that require enhancing regulatory T cell activity. Thus, it would require undue experimentation on the part of the skilled artisan to use the claimed method as recited, in the absence of sufficient information to predict the results with an adequate degree of certainty. In view of this unpredictability in the treatment of different conditions in which enhancing regulatory T cell activity is required, there cannot be said to be any reasonable expectation of success at the in vivo application of a potential therapy, especially in view of the fact that the current specification as filed presents no working examples pertaining to the method of treatment of all the various conditions in vivo. Therefore, a method as recited in claim 12 has not been enabled by the specification. Given the breadth of claim 12 in light of the predictability of the art as determined by the number of working examples, the level

of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of skill in the art to practice the claimed invention.

Claim rejections-35 U.S.C. 112, second paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 12, 15-17, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 is rejected as vague and indefinite for several reasons.

Claim 12, line 2, is vague and indefinite because it recites "medicament" rather than the conventional "a composition comprising….".

Claim 12, is improper because even though it is a method claim, it fails to recite steps in the claim.

Claim 12 is also vague and indefinite because it fails to recite a condition to be treated.

Claim 15 is rejected as vague and indefinite for several reasons.

Claim 15, line 2, is vague and indefinite because it recites "medicament" rather than the conventional "a composition comprising….".

Claim 15, lines 3-4, is vague and indefinite because it recites "condition characterised by inappropriate or undesirable T cell activation". The metes and bounds of the "condition" are unclear. Furthermore, the term "characterized" has been misspelled.

Claim 17, lines 2-3, is improper because it recites "arthritis (e.g. rheumatoid arthritis). Regarding claim 17, the phrase "e.g." renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Appropriate correction is required.

Claim 16 is rejected as vague and indefinite insofar as it depends on the above rejected claims for their limitations.

Claim rejections-35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4a. Claims 12, 15-16, are rejected under 35 U.S.C. 102(b) as being anticipated by Devergne et al. (WO 97/13859)

Devergne et al discloses a method for modulating the immune response in a subject by administering EBI3-p35 complex to a subject that has an autoimmune condition (see abstract; see page 4, lines 8-30). Therefore, the method described in the reference meets the limitations of instant claims 12, 15-16.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5a. Claim 17 is rejected under 35 U.S.C. 103(a) as unpatentable over Devergne et al. (WO 97/13859).

The reference teaches as set forth above in paragraph 4a but fails to specifically recite an autoimmune condition. However, it would be prima facie obvious to one of ordinary skill in the art to administer the EBI3-p35 protein in an inflammatory/autoimmune condition such as rheumatoid arthritis. One of ordinary skill in the art would have been motivated to do so because the reference teaches on page 4, lines 22-24, discloses "….the EBI3/p35 protein complex is administered to a subject that has an autoimmune condition to ameliorate the autoimmune

condition". Thus the artisan would have expected success administering EBI3-p35 for enhancing regulatory T cell activity in a subject for the treatment of rheumatoid arthritis.

Conclusion

Claims 12, 15-17 are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Prema Mertz/
Primary Examiner
Art Unit 1646